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Original Article

Sleep-disordered breathing and pulmonary function in obese children and adolescents

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ABSTRACT

Objective: Obese children have an increased risk of developing obstructive sleep apnea syndrome (OSAS) compared to normal-weight children. In obese children, OSAS is more frequently associated with oxygen desaturations, which might be caused by pulmonary function abnormalities. Our goal was to investigate the association between OSAS and pulmonary function in obese children and adolescents.
Methods: There were 185 children included and distributed in groups based on their obstructive apnea–hypopnea index (151 controls, 20 mild OSAS, and 14 moderate-to-severe OSAS). All subjects underwent polysomnography and pulmonary function testing.
Results: Several differences in pulmonary function were observed between groups. Vital capacity (VC) and forced expired volume in 1 s (FEV_1) were significantly decreased in patients with moderate-to-severe OSAS, as were expiratory reserve volume (ERV), total lung capacity, and functional residual capacity (FRC). Correlations between FEV_1, FRC, and ERV with OSAS severity remained significant independent of the degree of adiposity. Correlations between FEV_1/VC and sleep-related respiratory parameters did not persist after correction for adiposity.
Conclusion: An association between awake pulmonary function and sleep-related respiratory parameters could be observed in our population of obese children. These results suggest that OSAS severity is correlated with a diminished lung function. However, the level of obesity remains an important confounding factor in both OSAS severity and pulmonary function.

1. Introduction

The prevalence of childhood obesity is increasing worldwide and has been recognized as a major health problem associated with several physical, psychosocial, and social consequences [1]. Restrictive pulmonary function abnormalities are a well-reported complication of obesity in an adult population, with reductions in lung volumes and expiratory flow rates being most frequently reported [2]. However, similar studies in children show conflicting data and no strong evidence has been found for a correlation between the degree of obesity and pulmonary function abnormalities in children [3].

Sleep-disordered breathing (SDB) is a well-documented complication in obese adults and children. SDB includes primary snoring, upper airway resistance syndrome, and obstructive sleep apnea syndrome (OSAS) [4]. OSAS is defined by intermittent cycles of upper airway collapse associated with hypoxia and arousals during sleep. The prevalence of OSAS has been reported to be between 13% and 59% in obese children, compared to 2–3% in normal-weight children [5,6]. Multiple factors may be responsible for the increased risk of OSAS in obese children and adolescents, including structural changes in the upper airway, adenotonsillar hypertrophy, and excess fat deposition around the pharynx [7–9]. Other possible underlying mechanisms may be pulmonary function abnormalities. Obesity may result in central adiposity and an excess mechanical load on the chest wall, which in turn can result in reduced functional residual capacity (FRC) and tidal volumes [10]. A reduction in FRC can augment the development of severe hypoxia during OSAS. This could explain why OSAS in obese

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children is associated with more frequent oxygen desaturations. Several studies have examined whether pulmonary function tests (PFTs) are abnormal in adults with SBD [11–13]. However, these results have been inconsistent, possibly due to confounding factors such as chest wall abnormalities in obesity. Limited data are available concerning the association between obesity, SDB, and PFT in children. Therefore, our goal was to investigate the association between SDB and pulmonary function in obese children and adolescents, and the following hypotheses were examined: (i) diminished lung volumes are associated with an increased risk for obstructive events and (ii) OSAS is associated with a more obstructive breathing pattern, as measured by PFT.

2. Methods

2.1. Study population

In this prospective study, consecutive overweight and obese children were recruited between November 2006 and December 2012 at the Pediatric Obesity Clinic of the Antwerp University Hospital. Children were excluded in case of infection, chronic medical condition or genetic, neuromuscular, or craniofacial syndromes. The ethics committee of the Antwerp University Hospital approved this study and informed consent was obtained from the patients and their parents.

2.2. Anthropometry

All measurements were performed in the morning, after an overnight fast with patients undressed. Height, weight, waist circumference, and waist-to-hip ratio (WHR) were measured using standardized techniques by skilled personnel. Fat mass was measured with bioelectrical impedance analysis, using the Deurenberg formula for children [14]. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2) and was further analyzed as *z*-scores, using the Flemish growth study as a reference population [15]. Overweight and obesity were defined according to the International Obesity Task Force criteria [16].

2.3. Pulmonary function testing

All patients underwent full lung function evaluation. Lung function tests included spirometry and helium dilution (Jaeger MS-PFT analyzer unit, Jaeger, Würzburg, Germany), and full body plethysmography (Jaeger Masterscreen box, Jaeger, Würzburg, Germany). Spirometry yielded the following data: vital capacity (VC) and forced expired volume in 1 s (FEV_1). FRC, total lung capacity (TLC), and residual volume (RV) were measured via body plethysmography and helium dilution. Expiratory reserve volume (ERV) was calculated by means of FRC and RV measured by body plethysmography. Specific airway resistance (sRaw) was measured through body plethysmography. PFT parameters are expressed as a percentage of the predicted value.

2.4. Polysomnography

All children underwent nocturnal polysomnography for $\geqslant$6 h on the day of admission. The following variables were continuously measured and recorded by a computerized polysomnograph (Brain RT, OSG, Rumst, Belgium): electroencephalography (C4–Al and C3–A2); electrooculography; electromyography of anterior tibial and chin muscles; and electrocardiography. Respiratory effort was measured by respiratory inductance plethysmography and oxygen saturation by a finger probe connected to a pulse oximeter. Airflow was measured by means of a nasal pressure cannula and thermistor, and snoring was detected by means of a microphone at the suprasternal notch. All patients were monitored on audio/videotape using an infrared camera. Respiratory events were scored according to the American Academy of Sleep Medicine guidelines [17].

The obstructive apnea–hypopnea index (oAHI) was defined as the average number of obstructive apneas and hypopneas per hour of sleep. Mild OSAS was diagnosed by the presence of an oAHI between 2 and 5 and moderate-to-severe OSAS was defined by an oAHI $\geqslant$ 5. The respiratory disturbance index (RDI) was calculated as the sum of the recorded apneas and hypopneas divided by the total sleep time. All desaturations of $\geqslant$4% from the baseline oxygen saturation were quantified and the oxygen desaturation index (ODI) was calculated as the total number of desaturations divided by the total sleep time.

2.5. Statistical analysis

All statistical analysis was performed using SPSS 20.0 (SPSS, Chicago, IL, USA). A previous study showed a significant difference in FEV_1 between subjects with and without OSAS [18]. Based on that study, a sample size of 27 subjects with OSAS would be needed to achieve adequate statistical power (type I error rate of 5% and a power goal of 90%). Normality was tested by the Kolmogorov–Smirnov test. Normally distributed data are presented as mean ± standard deviation. Skewed data are reported as median ± interquartile range. Patients were distributed in groups based on their oAHI. Groups were compared by means of χ^2, one-way analysis of variance, or Kruskal–Wallis test, as appropriate. The differences between groups were further analyzed by means of the post hoc Tukey test or Jonckheere–Terpstra trend test as appropriate. Correlations between PFT and sleep parameters were calculated using Pearson's or Spearman's correlation analysis as appropriate. Linear regression analysis was performed in the case of a significant correlation to determine whether the correlation persisted after controlling for the degree of adiposity. Because the different measures of adiposity are highly intercorrelated, linear regression was done by the inclusion of one measure of adiposity with the highest univariate correlation coefficient for the respective outcome (BMI *z*-score, waist circumference, WHR, fat mass). For all analyses, $P < 0.05$ was considered statistically significant.

3. Results

3.1. Subjects' characteristics

A total of 185 overweight and obese children were included in this study with an average BMI of 30.4 kg/m^2 (range: 19.7–48.1 kg/m^2), which corresponds to a mean *z*-score of 2.4 (range: 1.5–3.6). Mean age was 12 years (range: 5–17 years) and 40% of subjects were male. OSAS was diagnosed in 34 children (18.3%), 20 subjects had mild OSAS (10.8%), and 14 moderate-to-severe OSAS (7.5%). Patient characteristics between the three groups (oAHI < 2; 2 < oAHI < 5; oAHI $\geqslant$ 5) are compared in Table 1. No significant difference in patient characteristics between groups was found except for WHR.

3.2. Respiratory parameters

Sleep-related respiratory parameters were significantly different between groups as expected. VC and FEV_1 were significantly lower in patients with OSAS, as were TLC and FRC measured by helium dilution. ERV was also significantly lower in patients with OSAS. Post-hoc testing showed a significant decrease for all lung

function parameters in patients with moderate-to-severe OSAS compared to patients without OSAS.

Several correlations were found between various sleep-related respiratory parameters and PFT (Table 2). Correlations between measures of adiposity (BMI *z*-score, fat mass, waist circumference, and WHR) and PFT are shown in Table 3. FEV_1 was positively correlated with mean oxygen saturation during sleep (SaO_2) and SaO_2 nadir. FEV_1 was also inversely correlated with the RDI. BMI *z*-score and fat mass were positively correlated with FEV_1. FEV_1/VC was positively correlated with mean SaO_2 and with WHR. There was a negative correlation between FEV_1/VC and waist circumference. RV and TLC did not correlate with any nocturnal respiratory parameters, but correlations were significant for measures of adiposity. FRC measured by body plethysmography correlated inversely with RDI and ODI. FRC measured by helium dilution was inversely correlated with oAHI. Both FRCs were also inversely correlated with waist circumference and WHR. ERV was inversely correlated with several nocturnal respiratory parameters (oAHI, RDI, and ODI), as well as with BMI *z*-score and fat mass. There was an inverse correlation between sRaw and SaO_2 nadir, but there were no correlations between sRaw and measures of adiposity.

There was no difference in the prevalence of asthma between groups ($P = 0.5$). However, children with asthma had a significantly lower SaO_2 nadir compared to children without asthma ($P = 0.04$). Furthermore, there was a trend for higher ODI in children with asthma ($P = 0.06$).

Table 1
Patient characteristics of subjects with and without obstructive sleep apnea.

	oAHI < 2	2 < oAHI < 5	oAHI ⩾ 5	*P*-value
Patient characteristics				
N	151	20	14	
Male/female	56/95	8/12	9/5	0.1
Age (years)	12 ± 3	11 ± 3	12 ± 3	0.3
Height (cm)	154.5 ± 22.5	150.5 ± 26.5	164.3 ± 22.1	0.2
Weight (kg)	68.8 ± 37.6	69.9 ± 46.2	88.7 ± 37.7	0.2
BMI *z*-score	2.5 ± 0.6	2.5 ± 0.6	2.6 ± 0.5	0.8
Waist (cm)	91.1 ± 14.2	92.7 ± 14.8	98.1 ± 15.8	0.2
WHR	0.88 ± 0.09	0.91 ± 0.08	0.94 ± 0.07	0.01
FM (%)	36.9 ± 4.1	36.1 ± 4.8	35.5 ± 3.5	0.8
Asthma (%)	13.9	5.0	14.3	0.5
Nocturnal respiratory parameters				
oAHI (events/h)	0.2 ± 0.6	3.4 ± 1.7	7.8 ± 13.3	<0.001
RDI (events/h)	1.3 ± 2.0	4.5 ± 2.2	10.0 ± 13.9	<0.001
Mean SaO_2 (%)	97.0 ± 1.4	96.8 ± 1.1	96.0 ± 1.8	0.06
SaO_2 nadir (%)	88.4 ± 10.0	91.2 ± 3.0	89.5 ± 61.8	0.04
TST_{95} (%)	99.5 ± 2.8	97.7 ± 5.3	91.5 ± 33.4	0.004
ODI (events/h)	0.6 ± 2.0	0.5 ± 2.2	1.2 ± 3.6	0.4
Awake pulmonary function				
VC (%pred)	106 ± 13	103 ± 13	95 ± 15	0.01
FEV_1 (%pred)	104 ± 13	101 ± 14	95 ± 17	0.05
FEV_1/VC (%pred)	99 ± 8	98 ± 7	101 ± 7	0.4
RV_{pleth} (%pred)	106 ± 35	111 ± 61	114 ± 45	0.4
TLC_{pleth} (%pred)	106 ± 13	107 ± 12	98 ± 13	0.08
FRC_{pleth} (%pred)	96 ± 21	95 ± 20	84 ± 31	0.1
ERV (%pred)	85 ± 31	72 ± 32	61 ± 28	0.008
RV_{He} (%pred)	89 ± 36	86 ± 35	85 ± 26	0.6
TLC_{He} (%pred)	101 ± 21	101 ± 11	91 ± 20	0.03
FRC_{He} (%pred)	82 ± 21	76 ± 31	65 ± 21	0.008
sRaw (kPa.s)	1.159 ± 0.502	1.189 ± 0.459	1.290 ± 0.520	0.5

BMI, body mass index; WHR, waist-to-hip ratio; FM, fat mass; oAHI, obstructive apnea–hypopnea index; RDI, respiratory disturbance index; SaO_2, oxygen saturation; TST_{95}, percentage of sleep time with an oxygen saturation >95%; ODI, oxygen desaturation index; VC, vital capacity; FEV_1, forced expired volume in 1 s; pleth, measured by means of body plethysmography; He, measured by means of helium dilution; RV, residual volume; TLC, total lung capacity; FRC, functional residual capacity; ERV, expiratory reserve volume; sRaw, specific airway resistance; %pred, percentage of the predicted value.
Results are presented as mean ± standard deviation or median ± interquartile range.

Table 2
Spearman correlation analysis between pulmonary function tests and sleep-related respiratory parameters.

	oAHI	RDI	Mean SaO_2	SaO_2 nadir	TST_{95}	ODI
VC	NS	NS	NS	NS	NS	NS
FEV_1	NS	−0.15	0.15	0.16	0.23	NS
FEV_1/VC	NS	NS	0.20	NS	0.21	NS
RV_{pleth}	NS	NS	NS	NS	NS	NS
TLC_{pleth}	NS	NS	NS	NS	NS	NS
FRC_{pleth}	NS	−0.15	NS	NS	0.27	−0.19
ERV	−0.19	−0.22	NS	NS	0.19	−0.19
RV_{He}	NS	NS	NS	NS	NS	NS
TLC_{He}	NS	NS	NS	NS	NS	NS
FRC_{He}	−0.24	NS	NS	NS	NS	NS
sRaw	NS	NS	NS	−0.19	NS	NS

oAHI, obstructive apnea–hypopnea index; RDI, respiratory disturbance index; SaO_2, oxygen saturation; TST_{95}, percentage of sleep time with an oxygen saturation >95%; ODI, oxygen desaturation index; VC, vital capacity; FEV_1, forced expired volume in 1 s; pleth, measured by means of body plethysmography; He, measured by means of helium dilution; RV, residual volume; TLC, total lung capacity; FRC, functional residual capacity; ERV, expiratory reserve volume; sRaw, specific airway resistance; NS, non-significant.
Significant Spearman correlation coefficients are shown.

Table 3
Spearman correlation analysis between pulmonary function tests and measures of adiposity.

	BMI *z*-score	Waist	WHR	FM
VC	0.19	0.18	NS	0.25
FEV_1	0.23	NS	NS	0.21
FEV_1/VC	NS	−0.18	0.15	NS
RV_{pleth}	NS	−0.27	NS	NS
TLC_{pleth}	0.18	NS	NS	0.17
FRC_{pleth}	NS	−0.32	−0.28	NS
ERV	−0.19	NS	−0.38	NS
RV_{He}	NS	−0.17	NS	NS
TLC_{He}	0.17	NS	NS	0.17
FRC_{He}	NS	−0.19	−0.24	NS
sRaw	NS	NS	NS	NS

BMI, body mass index; WHR, waist-to-hip ratio; FM, fat mass; VC, vital capacity; FEV_1, forced expired volume in 1 s; pleth, measured by means of body plethysmography; He, measured by means of helium dilution; RV, residual volume; TLC, total lung capacity; FRC, functional residual capacity; ERV, expiratory reserve volume; sRaw, specific airway resistance; NS, non-significant.
Significant Spearman correlation coefficients are shown.

3.3. Linear regression analysis

Linear regression analysis was performed if PFT correlated with both sleep-related respiratory parameters and measures of adiposity. Correlations between sleep-related respiratory parameters (RDI, mean SaO_2, SaO_2 nadir) and FEV_1 remained significant after correction for BMI *z*-score (Table 4). No correlations were found between FEV_1/VC and sleep-related respiratory parameters after correction for adiposity. FRC measured by body plethysmography remained significantly correlated with RDI ($r = -0.16$; $P = 0.03$)

Table 4
Results of linear regression analysis between FEV_1 and pulmonary function tests after correction for body mass index *z*-score.

FEV_1	*P*	*r*
RDI	<0.001	−0.28
Mean SaO_2	<0.001	0.29
SaO_2 nadir	0.003	0.22
TST_{95}	0.09	–

FEV_1, forced expired volume in 1 s; RDI, respiratory disturbance index; SaO_2, oxygen saturation; TST_{95}, percentage of sleep time with an oxygen saturation >95%.
Significant correlation coefficients are shown.

and ODI ($r = -0.16$; $P = 0.04$) after correction for waist circumference. The correlation between FRC measured by helium dilution and oAHI ($r = -0.17$; $P = 0.02$) was significant after correction for WHR. Correlations between ERV and oAHI ($r = -0.26$; $P = 0.001$), RDI ($r = -0.28$; $P < 0.001$) and ODI ($r = -0.17$; $P = 0.02$) also remained significant after correction for WHR.

4. Discussion

Pulmonary function was correlated with OSAS severity in this population of obese children and adolescents: increasing RDI and ODI correlated with diminished lung function, especially the indicators of flow limitation and FRC. Second, desaturation during sleep was associated with worse FEV_1. This suggests that pulmonary function abnormalities have a role in the pathology of OSAS, which means that improving pulmonary function may diminish the severity of OSAS.

FEV_1 correlated with several sleep parameters. Lower FEV_1 was correlated with a higher RDI, implying that patients with lower FEV_1 have more apneas and hypopneas. A similar result in adults was found by Zerah-Lancner et al. where FEV_1 decreased with a higher apnea–hypopnea index [19]. A significant difference in FEV_1 between groups was found in our population. Nonetheless, FEV_1 remained within normal ranges in all groups, implying that FEV_1 has no diagnostic value for OSAS. The decrease of FEV_1 may be due to a restrictive breathing pattern, which is evident by a corresponding decrease in TLC and FRC with OSAS severity and a constant FEV_1/VC. However, there is also evidence for an obstructive breathing pattern considering the inverse association between sRaw and SaO_2 nadir, which implies that patients with a high sRaw have more severe oxygen desaturations during the night, independent of the level of adiposity. A similar result was found by Zerah-Lancner et al., who studied a population of overweight adults and found an association between specific airway conductance and OSAS severity [19]. Furthermore, the correlation between FEV_1/VC and nocturnal respiratory parameters was due to a confounding effect of waist circumference, implying that adiposity, not OSAS severity is the main contributor to this association.

Airway inflammation plays a key role in the pathogenesis of OSAS, but the exact mechanism remains unknown. Upper airway inflammation was correlated with OSAS in several previous studies [20,21], but bronchial inflammation has also been demonstrated in adults and children with OSAS [18,22,23]. Underlying bronchial inflammation may explain the lower FEV_1 in patients with OSAS. Inflammatory airway diseases, such as asthma, have been linked to OSAS; studies have shown that OSAS is more frequent in children and adults with bronchial asthma [24–27], though we could not confirm this in our population. Nevertheless, patients with asthma are prone to have more frequent and severe oxygen desaturation during sleep, evident by the difference in SaO_2 nadir and ODI between subjects with and without asthma in our population.

FRC measured by helium dilution is significantly different between our groups. This could support the hypothesis that a reduction in FRC may mediate the development of more severe hypoxia during OSAS in obese children. Indeed, FRC is lowest in our group with moderate-to-severe OSAS. A difference in WHR was also found between groups, suggesting that central adiposity could play a role in the reduction of FRC. However, the association between oAHI and FRC remained significant after correcting for WHR. This could imply that central adiposity is not the only influencing factor and that other mechanisms could be at work. Central adiposity and OSAS could interact and influence each other's effect on pulmonary function. However, the effect of the interaction between WHR and oAHI on FRC was not significant ($P = 0.2$).

Two different methods were used for the measurement of lung volumes, namely full body plethysmography and helium dilution. Helium dilution measures actual ventilated lung volumes, in contrast to body plethysmography which also measures poorly ventilated areas. Nonetheless, correlation between FRC and OSAS severity was significant for both techniques. However, FRC measured by helium dilution was significantly lower in the group with moderate-to-severe OSAS, suggesting that actual lung volume may be a determining factor in OSAS severity. Lower lung volumes could relate to a less pronounced tethering effect on the upper airway, increasing the risk of obstructive events by increasing the critical dosing pressure (P_{crit}). The latter may be due to less caudal traction at the level of the trachea and the upper airway, which increases the transmural pressure and thus P_{crit}. Furthermore, a low FRC could also lead to ventilation inhomogeneity in obese children with OSAS or even without OSAS, and further research is warranted regarding this subject.

Respiratory problems are more frequently observed in obese children compared to their normal-weight peers. The associations of FRC and ERV with obesity are well known [28], and we confirmed this in our population. Low FRC and ERV are also associated with more desaturations during sleep in our population. However, this is a direct consequence of the level of obesity since the association did not persist after correction for waist or WHR. This indicates that central obesity is an important factor in the presence of desaturations during sleep. A possible mechanism is the presence of abdominal fat, which raises intra-abdominal pressure in the supine position resulting in a reduction in lung volumes, V/Q mismatch, and lower oxygen reserves. The combination of decreased lung volumes and increased airway resistance makes obese children more susceptible for oxygen desaturations during sleep.

Several limitations need to be considered. First, PFTs were only performed in a sitting position, and no supine pulmonary data were obtained. Second, dietary habits of the subjects were not acquired and therefore not included in the results. A final limitation is that most of our study population consisted of subjects without OSAS or with mild OSAS.

In conclusion, an association between awake pulmonary function and sleep-related respiratory parameters may be observed in our population of overweight and obese children and adolescents. Diminished lung volumes are associated with OSAS severity. FEV_1 is also correlated with OSAS severity, implying a possible role for airway inflammation in the pathology of OSAS. These results indicate that decreased pulmonary function, both obstructive and restrictive patterns, may contribute to the severity of OSAS in children. However, the level of obesity remains an important confounding factor in both OSAS severity and PFT.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.03.024.

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